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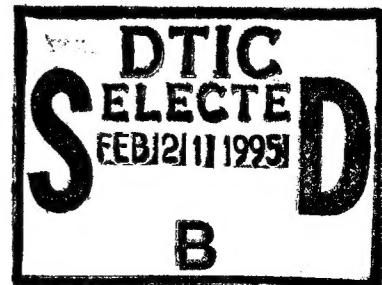
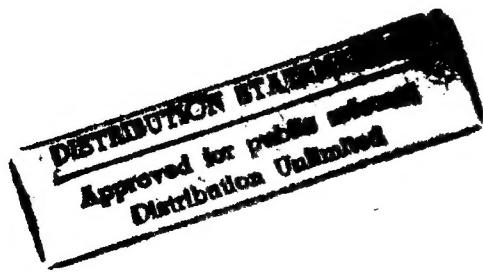
CARDIOVASCULAR CONTROL DURING STIMULATED HYPERGRAVITY

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<p>A model of the circulation was developed using anesthetized dogs which allowed blood pressures and flows at different levels of the body to be changed in ways that simulated the events occurring during acceleration. In particular the responses were examined to decreases in pressure to the carotid baroreceptors and increases in pressure in the splanchnic circulation, changes that would occur during + Gz acceleration. Splanchnic congestion was found to elicit reflex vasoconstriction in the splanchnic circulation itself as well as in the hind-limbs. There was an interaction between the effects of splanchnic distension and the carotid baroreceptor reflex resulting in nearly a doubling of the gain of the baroreflex. This research has defined a previously unknown mechanism which is likely to be of considerable importance in the maintenance of blood pressure during acceleration and could be of relevance to optimizing counter-G protection.</p>		
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This technical report has been reviewed and is approved for publication.

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A. OBJECTIVES OF THE RESEARCH

Acceleration forces which are experienced in high performance aircraft cause large changes in the pressure of blood in arteries and veins at different regions of the body. High levels of + Gz acceleration causes a decrease in pressure in the upper part of the body and engorgement of arteries and veins below the level of the hydrostatic indifference point. There are many control mechanisms in the body which are greatly influenced by the changes in the distribution of pressure and volume, and these interact to determine the overall responses of the cardiovascular system. Ultimately these cardiovascular reflexes are of considerable importance in determining an individual's tolerance to high levels of +Gz.

The main objective of our research was to analyse the various mechanisms which become disturbed during acceleration. It is expected that knowledge of the individual mechanisms which participate would allow us to predict the likely overall response to various combinations of stresses. The type of information required involves complex preparations to isolate the various reflexogenic areas and to determine the responses to changes in the levels of stimulation. This work is clearly impossible in man and even in experimental animals the degree of control that is required cannot be undertaken merely by use of intravascular instrumentation. For this reason we needed to devise an experimental animal model using acutely anesthetized preparations and to apply stimuli to the various regions in ways which would simulate the changes occurring during acceleration.

The following were the principal objectives of this research:

1. To develop a model, using anesthetized dogs, which allowed independent control of pressures or flows to regions of the body at various levels. The important regions were: the cerebral circulation; carotid baroreceptor region; chest level including coronary, ventricular and aortic baroreceptors; splanchnic circulation; hind limbs.
2. To determine the effects of setting baroreceptor pressures at different levels on the distensibility of the capacitance vessels.
3. To determine whether distension of the splanchnic capacitance vessels induces reflex vasoconstriction in splanchnic and other vascular beds.
4. To determine whether splanchnic distension interacts with the baroreceptor reflexes to change the gain of the baroreceptors.

These experiments essentially are the initial step in unraveling the mechanisms involved during acceleration. Further work will explore the possible ways in which the various mechanisms are integrated.

B. SUMMARY OF RESEARCH

1. Development of an animal model for independent control of pressures and flows at various levels of the body.

The preparation and some of the early experiments involving its use were published earlier this year (Self, Hainsworth, Krock, Doe & Latham, 1994).

A diagram of the preparation is shown in the attached paper (Self et al. 1994, Fig. 2). The technique involves dogs anesthetized with chloralose (100 mg/kg) and with the chest widely opened. The regions of the carotid sinuses were vascularly isolated and perfused at controlled pressures. The cerebral circulation was also perfused independently. A large cannula in the aortic arch facilitated the control of ventricular, coronary and aortic arch baroreceptors. The lumen of this cannula was connected to a pressure bottle and the pressure applied regulated ventricular and coronary arterial pressures. On the outside of the aortic cannula the aortic arch baroreceptors were controlled by a separate perfusion system.

The splanchnic circulation was perfused through the descending aorta above the diaphragm and the rate of perfusion determined splanchnic arterial pressure. The splanchnic circulation was drained through the inferior vena cava into a reservoir and splanchnic congestion could be achieved either by restricting the outflow by means of a "Starling" resistance or by applying pressure directly to the venous reservoir.

A hind-limb was vascularly isolated from the rest of the body, while maintaining its nerve supply intact. The limb was perfused through the femoral artery and drained from the femoral vein. This approach allowed us to use the limb either for applying a stimulus by increasing arterial or venous pressure, or for assessing the response to stimulation of receptors elsewhere. Distension receptors in the limb could be stimulated by increasing arterial inflow and/or by obstructing outflow. Responses in the limb were determined from changes in perfusion pressure when arterial inflow and venous draining pressure were held constant.

2. Effects of setting baroreceptor pressures at different levels on the distensibility of splanchnic capacitance vessels.

During + Gz acceleration, pressure to carotid baroreceptors decreases and the splanchnic circulation becomes congested. These experiments were undertaken to determine whether carotid hypotension, by causing reflex constriction of the splanchnic capacitance vessels, offers protection against excessive blood pooling in the splanchnic region.

Using the preparation described above, we held the carotid sinus pressure constant while the splanchnic circulation was congested by increasing the outflow resistance. Changes in splanchnic volume were determined by integration of the changes in venous outflow, while the arterial inflow remained constant. Venous obstruction caused the flow out of the region to decrease until the venous pressure increased sufficiently to overcome the obstruction. Graded increases in venous pressure allowed the determination of vascular compliance in the region. The effects of progressive venous distension were determined at high and low constant levels of carotid sinus pressure. Decreasing carotid pressure caused a decrease in the volume of blood in the splanchnic region, but this effect was counteracted by a paradoxical increase in compliance. These results imply that carotid sinus hypotension may provide some protection against loss of effective circulating blood into the splanchnic capacitance vessels. However, this benefit is lost as the vessels become distended at high pressures.

3. Reflex responses to distension of the splanchnic circulation

Acceleration stress causes distension of splanchnic vessels particularly the veins, and we carried out experiments to determine whether this gave rise to protective reflex responses. In our simulation we

distended the splanchnic vessels by either applying a positive pressure to the venous reservoir or by restricting vena caval outflow. This reduced or stopped the outflow until venous pressure achieved the required level. These experiments showed that venous distension did cause an increase in arterial resistance. This was seen not only in the splanchnic circulation itself where the perfusion pressure increased far more than the applied change in venous pressure, but also in an isolated perfused limb in which the splanchnic venous distension could have had no direct effect (Fig 1).

4. Interaction between effects of splanchnic congestion and baroreceptor reflex

The preparation was similar to that described in (3) above. Two types of experiments were undertaken. In one, carotid pressure was held at different levels while the responses were studied to graded splanchnic venous distension. In the other, the responses to stepwise changes in baroreceptor pressure were determined, at different levels of splanchnic venous distending pressure.

Both types of experiments showed that there was an important interaction between the two reflexogenic areas. At a high carotid pressure, both the limb and the splanchnic resistance vessels dilated and they did not constrict to increases in splanchnic venous pressure. However, at the low carotid pressure, not only was there a powerful vasoconstriction but that the vasoconstriction increased even more when the splanchnic veins were congested. The results of the experiments of the responses to stepwise changes in carotid pressure were compatible with this: increasing splanchnic venous pressure nearly doubled the gain of the carotid sinus reflex (Fig. 2).

The mechanism of this interaction still needs to be worked out. However, it has demonstrated for the first time a potentially very important regulating mechanism. Gravitational stress decreases the stimulus to carotid baroreceptors and increases splanchnic distension. The two mechanisms together interact to potentiate and thereby to cause a greater degree of vasoconstriction than would be produced by either mechanism alone.

We do not yet know whether the reflex from the splanchnic region is a response to venous distension or to venous pressure. This is of potential importance because the modern anti-G devices are very effective in limiting venous distension but very large changes in venous pressure are likely. Further studies to evaluate the precise nature of this reflex are planned. In particular we propose to determine the effects of changes in venous pressure when distension is limited.

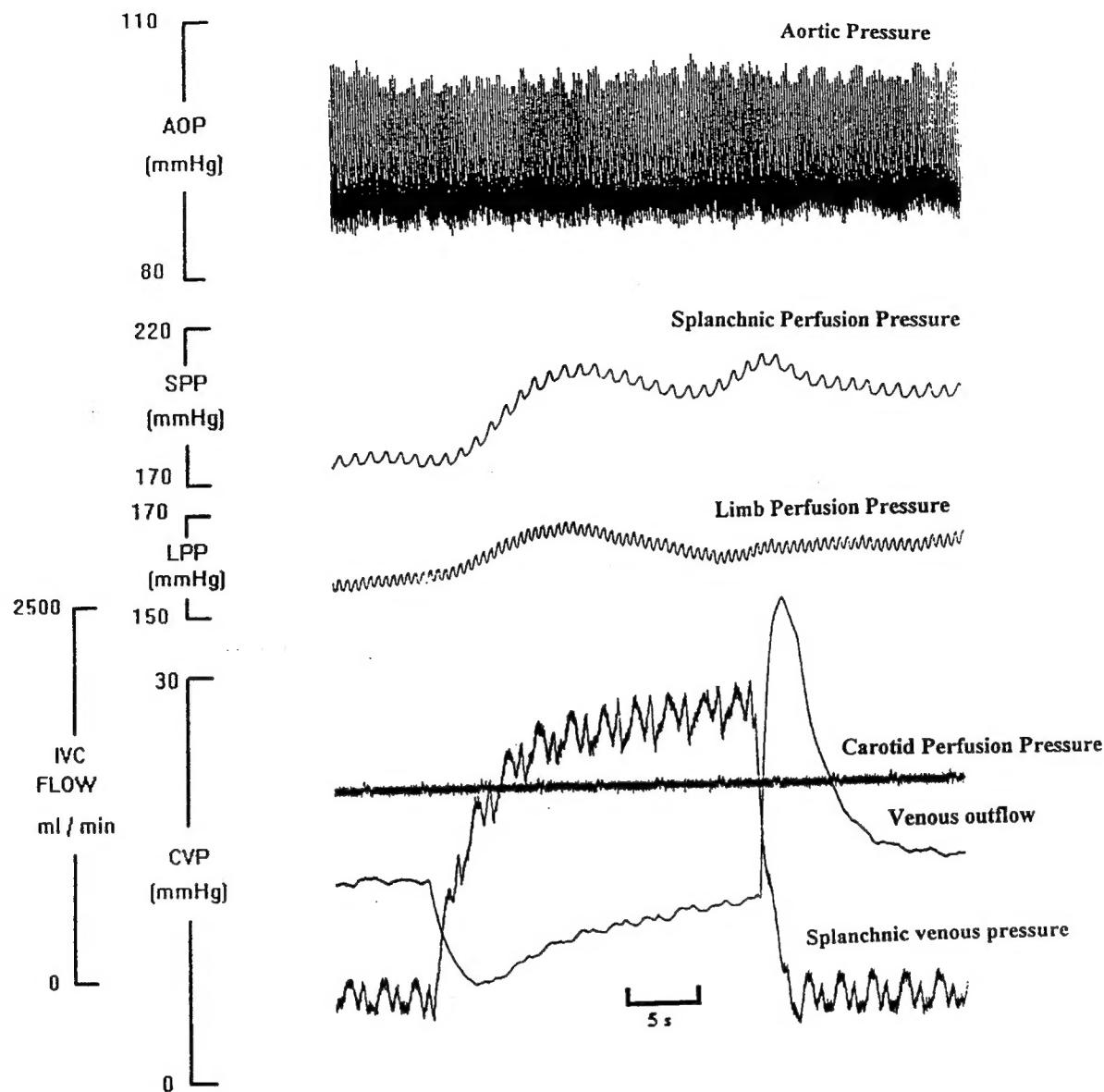


Fig 1. Responses to splanchnic venous distension. Traces are of aortic arch pressure (held constant), splanchnic and hind-limb perfusion pressures (flow constant; vascular resistance therefore related to pressure), carotid sinus pressure (held constant at 60 mmHg), outflow from inferior vena cava and splanchnic venous pressure.

Tests show that restriction of venous outflow which is associated with an increase in venous pressure causes increases in splanchnic and limb perfusion pressures. The change in splanchnic pressure was greater than the change in venous pressure and the limb was vascularly isolated, so these responses signify reflex vasoconstriction.

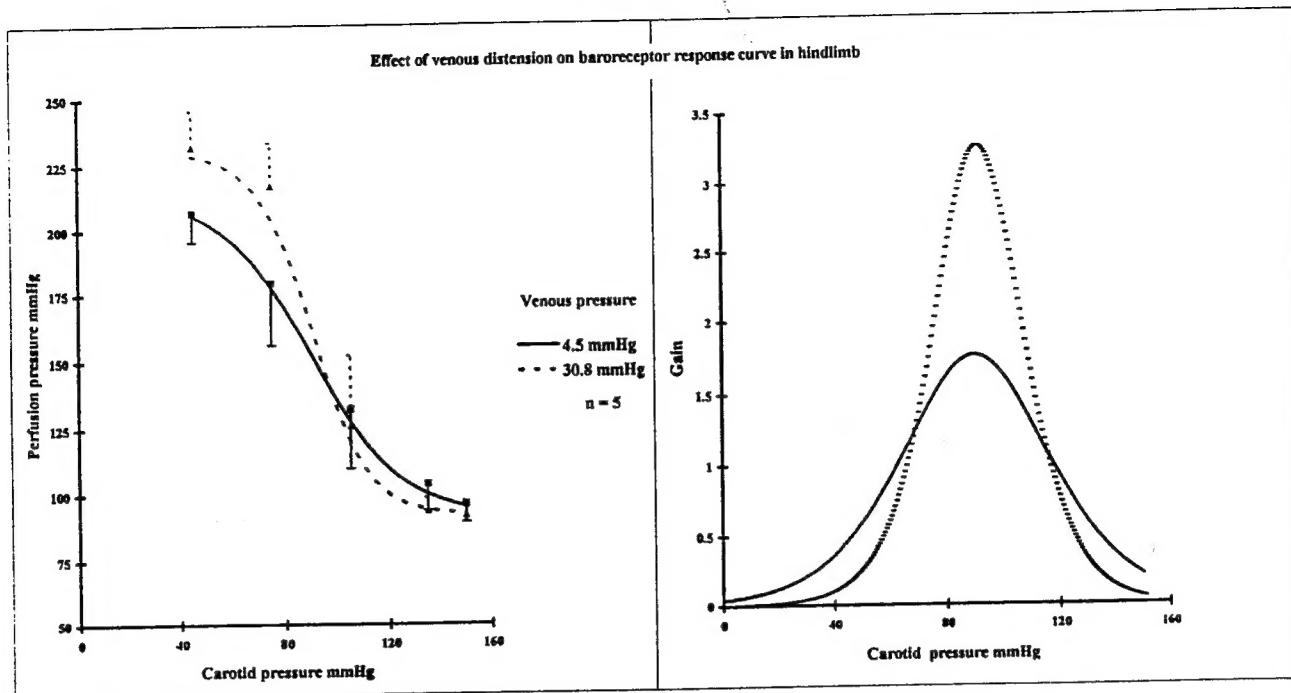


Fig 2. Effects of distension of splanchnic veins on the response in the hind limb to changes in carotid sinus pressure. Results are means \pm SE from 5 dogs. Splanchnic distension increased the limb perfusion pressure at low carotid pressure and also increased the slope of the curve. The plot on the right is the differential of that on the left and shows that the peak gain of the reflex was nearly doubled at the low carotid pressure compared to that at the high pressure.

C. PUBLICATIONS

Papers already published.

Self, D.A., Hainsworth, R., Krock, L.P., Doe, C.P.A., and Latham, R.D. An acute animal model that simulates the hemodynamic situation present during +Gz acceleration. Aviat. Space, Environ. Med. 1994; 65: A80-A89.

Hainsworth, R. Self, D.A., Krock, L.P. and Doe, C.P.A. Reflex vascular responses to simulated orthostatic stress. Aviat. Space, Environ. Med. 1994; Abst. Aerospace Med. Assoc.

Doe, C.P.A., Self, D.A., Drinkhill, M.J., Myers, D.S. and Hainsworth, R. A mechanism for enhancement of vasoconstriction during gravitational stress. J. Physiol. Proc. Aberdeen Meeting 1994, C23.

Papers in preparation

Doe, C.P.A., Self, D.A., Drinkhill, M.J., Myers, D.S. and Hainsworth, R. The effects of splanchnic venous distension on the responses to stimulation of carotid sinus baroreceptors. To be submitted to Am. J. Physiology.

Drinkhill, M.J., Self, D.A., Doe, C.P.A., Myers, D.S. and Hainsworth, R. The effects of carotid baroreceptors on compliance and capacitance in the splanchnic circulation. To be submitted to Aviation. Space Environ. Med.

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